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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,526	06/19/2001	David Meeker	07680.0019.00000	2532

22852 7590 08/10/2005

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EXAMINER	
CHEN, SHIN LIN	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/884,526	MEEKER ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-19* is/are pending in the application.

4a) Of the above claim(s) *2,3 and 7-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 6 and 13-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed 5-27-05 has been entered. Claims 1 and 4 have been amended. Claims 1-4 and 6-19 are pending. Claims 1, 4, 6 and 13-19 are under consideration.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 4, 6 and 13-19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Schiffmann et al., January 2000 (PNAS, Vol. 97, No. 1, p. 365-370) or Desnick et al., 1979 (PNAS, Vol. 76, No. 10, pp. 5326-5330) each in view of Ziegler et al., 1999 (Human Gene Therapy, Vol. 10, No. 10, p. 1667-1682) and Selden et al., 1998 (WO 98/11206) and is repeated for the reasons set forth in the preceding Official action mailed 1-31-05. Applicant's arguments filed 5-27-05 have been fully considered but they are not persuasive.

Applicants argue that there is no motivation to combine the cited references and neither Desnick and Shiffmann teaches treatment of Fabry disease by gene therapy or with small molecule of any kind nor points out any defect of its teachings. Ziegler teaches combination of adenoviral vector and immunosuppressant but there is no motivation to combine Ziegler with either Desnick or Shiffmann because no immunological side effects associated with enzyme replacement therapy have been observed. Applicants further argue that Selden teaches the treatment of Fabry disease either with genetically modified human cells or with purified human alpha-gal A and, similar to Ziegler, there is no motivation to combine Selden with Desnick or Shiffmann (amendment, p. 6-10). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 1-31-05. Either Shiffmann or Desnick teaches treating Fabry disease with purified alpha-galactosidase A enzyme with success by decreasing the concentration of globotriaosylceramide in the treated subject. Ziegler teaches injection of an adenoviral vector encoding human alpha-galactosidase A (Ad2/CEHalpha-Gal) intravenously into Fabry knockout mice and shows that alpha-galactosidase A activity is elevated in all tissues of the injected Fabry mice and significant reduction in GL-3 (globotriaosylceramide) content in all tissues is concomitant with the increase in enzyme activity. Either Shiffmann or Desnick and Ziegler show the success of treating Fabry disease by reducing the concentration of GL-3 either by enzyme therapy or by gene therapy. Selden teaches that a patient with Fabry disease can be treated with either genetically modified human cells overexpressing and secreting human alpha-gal A (gene therapy) or with purified human alpha-gal A recombinant protein (enzyme replacement therapy) (e.g. p. 2 lines16-32). Selden reports some advantages of gene therapy over enzyme replacement therapy, however, Selden states that "individuals with alpha-gal A

deficiencies may also be treated with purified alpha-gal A (i.e. enzyme replacement therapy)". Thus, in view of the teachings of either Desnick or Shiffmann, and the teaching of Ziegler and Selden, one of ordinary skill in the art at the time of the invention would have been motivated to combine gene therapy and enzyme replacement therapy for treating Fabry disease because either gene therapy or enzyme replacement therapy can be used to treat Fabry disease according to the teachings of Desnick, Shiffmann and Ziegler, and Selden teaches using gene therapy for treating Fabry disease and individuals with alpha-gal A deficiencies may also be treated with purified alpha-gal A. One of ordinary skill also would have been motivated to combine alpha-galactosidase A protein and a vector encoding said protein in order as to obtain greater reduction of globotriaosylceramide level in a subject with Fabry disease since either administration of alpha-galactosidase A protein or a vector encoding alpha-galactosidase A can reduce globotriaosylceramide level in a subject with Fabry disease. Whether or not one of ordinary skill in the art would use immunosuppressant in combination with gene therapy is irrelevant to the motivation of one of ordinary skill to combine the teachings of Desnick or Shiffmann and Ziegler because of the reasons as discussed above.

It should be noted that the elected invention, i.e. a method of combination therapy for treatment of a subject having Fabry disease comprising the combination of gene therapy and enzyme replacement therapy, as indicated in Paper No. 8 was under consideration in the previous Official actions. Therefore, the subject matter of a method of reducing the accumulation of globotriaosylceramide in a subject by administering a alpha-galactosidase A protein and a vector encoding alpha-galactosidase A is being considered by examiner (also see Official action mailed 8-25-04).

Applicants argue that Selden repeatedly uses "or" to distinguish two potential methods of treatment (1) gene therapy, or (2) enzyme replacement therapy but fails to mention combination of gene therapy and enzyme replacement therapy (amendment, p. 10-11). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 1-31-05 and the reasons set forth above. Selden teaches using gene therapy for treating Fabry disease and implies that individuals with alpha-gal A deficiencies may also be treated with purified alpha-gal A. Even if Selden does not specifically points out combination of gene therapy and enzyme replacement therapy for Fabry disease, however, since either administration of alpha-galactosidase A protein or a vector encoding alpha-galactosidase A can reduce globotriaosylceramide level in a subject with Fabry disease, it would have been obvious for one of ordinary skill to combine alpha-galactosidase A protein and a vector encoding said protein so as to obtain greater reduction of globotriaosylceramide level in a subject with Fabry disease.

Applicants argue that the combined references do not teach or support the limitation of using a small molecule that inhibits upstream generation of lysosomal hydrolase substrate (amendment, p. 11-15). As discussed above, the elected invention is a method of combination therapy for treatment of a subject having Fabry disease comprising the combination of gene therapy and enzyme replacement therapy, as indicated in Paper No. 8. Therefore, the subject matter of a method of reducing the accumulation of globotriaosylceramide in a subject by administering a alpha-galactosidase A protein and a vector encoding alpha-galactosidase A is being considered by examiner. The use of a small molecule that inhibits upstream generation of lysosomal hydrolase substrate is irrelevant to the examined subject matter of the present invention. Thus, claims 1, 4, 6 and 13-19 remain rejected under 35 U.S.C. 103(a).

Conclusion

No claim is allowed.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER